

CLAIMS

1. A method of determining whether a tumor is metastatic, comprising comparing the level of expression of a gene in said tumor compared to a control value, wherein said gene is selected from the group consisting of DDOST, GNS, NEDD8, LOC51096, CCT5, CCT3, PPP2R1B and two ESTs (GENBANKTM Accession Nos. AA533633 and AI755112) and wherein an increase in the level of expression in said tumor compared to said control value indicates that the tumor is metastatic.
2. A method of determining whether a tumor is metastatic, comprising comparing the level of expression of a gene in said tumor compared to a control value, wherein said gene is selected from the group consisting of UBQLN1, AIM2, and USP9X and wherein a decrease in the level of expression in said tumor compared to said control value indicates that the tumor is metastatic.
3. The method of claim 1 or 2, wherein the expression level is determined by any one methods selected from group consisting of:
 - (a) detecting the mRNA of the genes
 - (b) detecting the protein comprising the amino acid sequence encoded by the genes, and
 - (c) detecting the biological activity of the protein comprising the amino acid sequence encoded by the genes
4. A method of diagnosing intestinal-type gastric cancer in a subject, the method comprising the steps of:
 - (a) detecting an expression level of one or more marker genes in a specimen collected from a subject to be diagnosed, wherein the one or more marker genes is selected from the group consisting of the genes listed in Table 1 and the genes listed in Table 2; and
 - (b) comparing the expression level of the one or more marker genes to that of a control, wherein high expression level of a marker gene from Table 1 or a low expression level of a marker gene from Table 2, as compared to control, is indicative of intestinal-type gastric cancer.

5. A method of predicting lymph node-negative cancers and lymph node-positive cancers, the method comprising the steps of:

(a) detecting an expression level of one or more marker genes in a specimen collected from a subject to be predicted, wherein the one or more marker genes is selected from the group consisting of DDOST, GNS, NEDD8, LOC51096, CCT5, CCT3, PPP2R1B, two ESTs (GENBANK Accession Nos. AA533633 and AI755112), UBQLN1, AIM2, and USP9X; and

(b) comparing the expression level of the one or more marker genes to that of a control, wherein a high expression level or low expression level of a marker gene selected from the group consisting of DDOST, GNS, NEDD8, LOC51096, CCT5, CCT3, PPP2R1B, and two ESTs (GENBANK Accession Nos. AA533633 and AI755112), as compared to the control, is indicative of lymph node-positive cancers or lymph node-negative cancers, respectively, or wherein a low expression level or high expression level of a marker gene selected from the group consisting of UBQLN1, AIM2, and USP9X, as compared to the control, is indicative of lymph node-positive cancers or lymph node-negative cancers.

6. The method of claim 5, wherein the marker gene to be selected is at least one gene selected from the group consisting of DDOST, GNS, NEDD8, LOC51096, and AIM2.

7. The method of claim 6, wherein the marker genes comprise all of DDOST, GNS, NEDD8, LOC51096, and AIM2.

8. The method of claim 7, wherein step (b) further comprises the steps of determining a function of the log ratios of the expression profiles over the selected genes comprising summing the weighted log ratios of the expression profiles over the selected genes, wherein the weight for each gene is a first value when the average log ratio is higher for lymph node-positive cancers than for lymph node-negative cancers and a second value when the average log ratio is lower for lymph node-negative cancers than for lymph node-positive cancers.

9. The method of any one of claim 1-5, wherein the expression level is determined by any one methods selected from group consisting of:

(a) detecting the mRNA of the genes

(b) detecting the protein comprising the amino acid sequence encoded by the genes, and

(c) detecting the biological activity of the protein comprising the amino acid sequence encoded by the genes

10. The method of claim 9, wherein the expression level of the one or more marker genes is determined by following steps of:

- 5 (a) synthesizing aRNA or cDNA of the marker genes from a specimen;
(b) hybridizing the aRNA or cDNA with probes for marker genes; and
(c) detecting the hybridized aRNA or cDNA with the probes quantifying the amount of mRNA thereof.

11. The method of claim 10, wherein the probes are fixed on a DNA array.

10 12. A method of screening for a therapeutic agent useful in treating or preventing intestinal-type gastric cancer, said method comprising the steps of:

(a) contacting a candidate compound with a cell expressing one or more marker genes, wherein the one or more marker genes is selected from the group consisting of the genes listed in Table 1 and Table 2; and

15 (b) selecting a compound that reduces the expression level of one or more of the up-regulated marker genes shown in Table 1, as compared to a control, or enhances the expression of one or more of the down-regulated marker genes shown in Table 2, as compared to a control.

20 13. A method of screening for a therapeutic agent useful in treating intestinal-type gastric cancer, said method comprising the steps of:

(a) administering a candidate compound to a test animal;
(b) measuring the expression level of one or more marker genes in a biological sample from the test animal, wherein the one or more marker genes is selected from the group consisting of the genes listed in Table 1 and Table 2;

25 (c) selecting a compound that reduces the expression level of one or more of the up-regulated marker genes shown in Table 1, as compared to a control, or enhances the expression of one or more of the down-regulated marker genes shown in Table 2, as compared to a control.

30 14. A method of screening for a therapeutic agent useful in treating intestinal-type gastric cancer, said method comprising the steps of:

(a) contacting a candidate compound with a cell into which a vector comprising the transcriptional regulatory region of one or more marker genes and a reporter gene

that is expressed under the control of the transcriptional regulatory region has been introduced, wherein the one or more marker genes are selected from the group consisting of the genes listed in Table 1 and Table 2;

(b) measuring the activity of said reporter gene; and

5 (c) selecting a compound that reduces the expression level of said reporter gene when said marker gene is an up-regulated marker gene selected from Table 1, or that enhances the expression level of said reporter gene when said marker gene is a down-regulated marker gene selected from Table 2, as compared to a control.

10 15.A method of screening for a therapeutic agent useful in treating intestinal-type gastric cancer, said method comprising the steps of:

(a) contacting a candidate compound with a protein encoded by a marker gene, wherein the marker gene is selected from the group consisting of the genes listed in Table 1 and Table 2;

(b) measuring the activity of said protein; and

15 (c) selecting a compound that reduces the activity of said protein when said marker gene is an up-regulated marker gene selected from Table 1, or that enhances the activity of said protein when said marker gene is a down-regulated marker gene selected from Table 2.

20 16. The method of any one of claims 12-15, wherein the marker gene is selected from the group consisting of the genes listed in Table 1.

17. The method of any one of claims 12-15, wherein the marker gene is selected from the group consisting of the genes listed in Table 2.

25 18. A method for treating or preventing intestinal-type gastric cancer, said method comprising the step of administering a compound that is obtained by the method according to any one of claims 12-15.

19. A method for treating or preventing intestinal-type gastric cancer in a subject, said method comprising the step of administering to the subject an antisense nucleic acids or an siRNA against an up-regulated marker gene, wherein said up-regulated marker gene is selected from the group consisting of the genes listed in Table 1.

30 20. A method for treating or preventing intestinal-type gastric cancer in an subject, said method comprising the step of administering to the subject an antibody or fragment thereof that binds to a protein encoded by an up-regulated marker gene, wherein said

up-regulated marker gene is selected from the group consisting of the genes listed in Table 1.

21. A method of treating or preventing intestinal-type gastric cancer in a subject, said method comprising the step of administering to the subject a down-regulated marker gene, or a protein encoded by the gene, wherein said down-regulated marker gene is selected from the group consisting of genes listed in Table 2.
22. A vaccine composition for treating or preventing a intestinal-type gastric tumor, wherein the vaccine composition comprises one or more components selected from the group consisting of:
- (a) DNA corresponding to one or more up-regulated marker genes selected from the group consisting of the genes listed in Table 1,
 - (b) a protein encoded by a DNA of described in (a) above, and
 - (c) an antigenic fragment of a protein described in (b) above.
23. A method for vaccinating a subject against intestinal-type gastric cancer, the method comprising the step of administering, either alone, or in combination:
- (a) a DNA corresponding to one or more up-regulated marker genes selected from the group consisting of the genes listed in Table 1,
 - (b) a protein encoded by a DNA described in (a) above, or
 - (c) an antigenic fragment of a protein described in (b) above.